

## CLAIMS

1. A freeze-dried interferon- $\gamma$  composition for transpulmonary administration having the following properties (i) to (iv):

- 5 (i) containing at least one hydrophobic stabilizer selected from the group consisting of hydrophobic amino acids, dipeptides of hydrophobic amino acids, tripeptides of hydrophobic amino acids and derivatives of hydrophobic amino acids and salts thereof; at least one hydrophilic stabilizer selected from the group consisting  
10 of hydrophilic amino acids, dipeptides of hydrophilic amino acids, tripeptides of hydrophilic amino acids, derivatives of hydrophilic amino acids and salts thereof; and interferon- $\gamma$   
(ii) a non-powder cake-like form;  
(iii) a disintegration index of 0.015 or more; and  
15 (iv) becoming fine particles having a mean particle diameter of 10 microns or less or a fine particle fraction of 10% or more upon receipt of an air impact having an air speed of at least 1 m/sec and an air flow rate of at least 17 ml/sec.

2. The freeze-dried interferon- $\gamma$  composition according  
20 to Claim 1, wherein the hydrophilic stabilizer is at least one selected from the group consisting of basic amino acids, neutral hydroxy amino acids, dipeptides of these amino acids, tripeptides of these amino acids, derivatives of these amino acids and salts thereof.

25 3. The freeze-dried interferon- $\gamma$  composition according

to Claim 1, wherein the hydrophilic stabilizer is at least one selected from the group consisting of basic amino acids, dipeptides of basic amino acids, tripeptides of basic amino acids, derivatives of basic amino acids and salts thereof.

5           4.       The freeze-dried interferon- $\gamma$  composition according to Claim 1, wherein the hydrophilic stabilizer is at least one selected from the group consisting of neutral hydroxy amino acids, dipeptides of neutral hydroxy amino acids, tripeptides of neutral hydroxy amino acids, derivatives of neutral hydroxy amino acids  
10       and salts thereof.

          5.       The freeze-dried interferon- $\gamma$  composition according to Claim 1, wherein the hydrophilic stabilizer is at least one selected from the group consisting of arginine, lysine, histidine, threonine, dipeptide of these amino acids, tripeptides of these  
15       amino acids, derivatives of these amino acids and salts thereof.

          6.       The freeze-dried interferon- $\gamma$  composition according to Claim 1, wherein the hydrophobic stabilizer is at least one selected from the group consisting of hydrophobic amino acids, dipeptides of hydrophobic amino acids, tripeptides of hydrophobic  
20       amino acids, derivatives of hydrophobic amino acids and salts thereof.

          7.       The freeze-dried interferon- $\gamma$  composition according to Claim 1, wherein the hydrophobic stabilizer is at least one selected from the group consisting of valine, leucine, isoleucine,  
25       phenylalanine and salts thereof.

8. The freeze-dried interferon- $\gamma$  composition according to Claim 1, wherein the content of the hydrophilic stabilizer is 1 to 500 parts by weight per 100 parts by weight of the hydrophobic stabilizer.

5 9. The freeze-dried interferon- $\gamma$  composition according to Claim 1, wherein the disintegration index is 0.02 or more.

10. The freeze-dried interferon- $\gamma$  composition according to Claim 1, wherein the disintegration index is from 0.015 to 1.5.

10 11. The freeze-dried interferon- $\gamma$  composition according to Claim 1, becoming fine particles having a mean particle diameter of 10 microns or less or a fine particle fraction of 10% or more upon receipt of an air impact having an air speed of at least 2 m/sec and an air flow rate of at least 17 ml/sec.

15 12. The freeze-dried interferon- $\gamma$  composition according to Claim 1, becoming fine particles having a mean particle diameter of 10 microns or less or a fine particle fraction of 10% or more upon receipt of an air impact having an air speed of at least 1 m/sec and an air flow rate of at least 20 ml/sec.

20 13. The freeze-dried interferon- $\gamma$  composition according to Claim 1, becoming fine particles having a mean particle diameter of 5 microns or less or a fine particle fraction of 20% or more upon receipt of the air impact.

25 14. The freeze-dried interferon- $\gamma$  composition for transpulmonary administration according to Claim 1, having the following properties (i) to (iv):

(i) containing at least one hydrophobic stabilizer selected from the group consisting of hydrophobic amino acids, dipeptides of hydrophobic amino acids, tripeptides of hydrophobic amino acids, derivatives of hydrophobic amino acids and salts thereof; at least  
5 one hydrophilic stabilizer selected from the group consisting of hydrophilic amino acids, dipeptides of hydrophilic amino acids, tripeptides of hydrophilic amino acids, derivatives of hydrophilic amino acids and salts thereof; and interferon- $\gamma$ ;

(ii) a non-powder cake-like form;

10 (iii) a disintegration index of 0.015 to 1.5; and

(iv) becoming fine particles having a mean particle diameter of 10 microns or less or a fine particle fraction of 10% or more upon receipt of an air impact having an air speed in the range of 1 to 300 m/sec and an air flow rate in the range of 17 ml/sec  
15 to 15 L/sec.

15. A dry powder interferon- $\gamma$  inhalation system for transpulmonary administration, using a combination of:

(1) a vessel housing the freeze-dried interferon- $\gamma$  composition for transpulmonary administration according to any  
20 of Claims 1 to 14; and

(2) a device comprising means capable of applying an air impact having an air speed of at least 1 m/sec and an air flow rate of at least 17 ml/sec to the freeze-dried composition in said vessel, and means for discharging the powder-form freeze-dried  
25 composition that has been made into fine particles.

16. The dry powder interferon- $\gamma$  inhalation system for transpulmonary administration according to Claim 15, wherein the vessel and the device are used in combination at the time of inhalation.

5 17. The dry powder interferon- $\gamma$  inhalation system for transpulmonary administration according to Claim 15, wherein the device is:

1) a dry powder inhaler for transpulmonary administration, being a device used for making a freeze-dried composition that  
10 has been housed in non-powder form in a vessel into fine particles, and administering the resulting fine particles to a user by inhalation,

comprising a needle part having an air jet flow path, a needle part having a discharge flow path, air pressure-feeding means for  
15 feeding air into the air jet flow path of said needle part, and an inhalation port that communicates with the discharge flow path of said needle part,

and characterized by being constituted such that a stopper that seals up said vessel is pierced by said needle parts, thus  
20 communicating the air jet flow path and the discharge flow path with the inside of said vessel, and air is jetted into said vessel through said air jet flow path using said air pressure-feeding means, thus making said freeze-dried composition into fine  
25 particles by the impact of the jetted air, and discharging the fine particles obtained from the inhalation port via said discharge

flow path, or

ii) a dry powder inhaler for transpulmonary administration, being a device used for making a freeze-dried composition that has been housed in non-powder form in a vessel into fine particles, and administering the resulting fine particles to a user by inhalation,

comprising a needle part having a suction flow path, a needle part having an air introduction flow path, and an inhalation port that communicates with said suction flow path,

and characterized by being constituted such that, in a state in which a stopper sealing up said vessel has been pierced by said needle parts, through the inhalation pressure of the user, air in said vessel is inhaled from said inhalation port, and at the same time outside air flows into said vessel, at a negative pressure, through said air introduction flow path, and as a result said freeze-dried composition is made into fine particles by the impact of the air flowing in, and the fine particles obtained are discharged from the inhalation port through said suction flow path.

18. The dry powder interferon- $\gamma$  inhalation system for transpulmonary administration according to Claim 15, using a combination of:

(1) containing a vessel housing the freeze-dried interferon- $\gamma$  composition for transpulmonary administration according to Claim 14; and

(2) a device comprising means capable of applying said air

impact to the freeze-dried composition in said vessel, and means for discharging the powder-form freeze-dried composition that has been made into fine particles.

19. A method of manufacturing a dry powdered interferon- $\gamma$  preparation for transpulmonary administration, comprising:

introducing air into a vessel to apply to a freeze-dried composition containing a single dose of interferon- $\gamma$  according to any of Claims 1 to 14 an air impact having an air speed of at least 1 m/sec and an air flow rate of at least 17 ml/sec using a device capable of applying said air impact to the freeze-dried composition in the vessel,

thereby making said freeze-dried composition into fine particles having a mean particle diameter of 10 microns or less or a fine particle fraction of 10% or more.

20. The method of manufacturing a dry powdered interferon- $\gamma$  preparation for transpulmonary administration according to Claim 19, wherein the fine particles prepared have a mean particle diameter of 5 microns or less or a fine particle fraction of 20% or more.

21. The method of manufacturing a dry powdered interferon- $\gamma$  preparation for transpulmonary administration according to Claim 19, carried out by using a device having means capable of applying an air impact having an air speed of at least 2 m/sec and an air flow rate of at least 17 ml/sec to the freeze-dried composition in the vessel, and introducing air having the air impact

into the vessel housing the freeze-dried composition.

22. The method of manufacturing a dry powdered interferon- $\gamma$  preparation for transpulmonary administration according to Claim 19, comprising:

5 introducing air into a vessel to apply to a freeze-dried composition containing a single dose of interferon- $\gamma$  according to Claim 14 an air impact having an air speed of 1 to 300 m/sec and an air flow rate of at least 17 ml/sec to 15L/sec using a device capable of applying said air impact to the freeze-dried composition  
10 in the vessel,

thereby making said freeze-dried composition into fine particles having a mean particle diameter of 10 microns or less or a fine particle fraction of 10% or more.

23. A transpulmonary administration method comprising:

15 making the freeze-dried interferon- $\gamma$  composition for transpulmonary administration containing a single dose of interferon- $\gamma$  according to any of Claims 1 to 14 into fine particles having a mean particle diameter of 10 microns or less or a fine particle fraction of 10% or more by applying an air impact having  
20 an air speed of at least 1 m/sec and an air flow rate of at least 17 ml/sec to the freeze-dried composition at the time of use, and administering the resulting fine particle powder to a user by inhalation.

24. The transpulmonary administration method according  
25 to Claim 23, wherein the freeze-dried interferon- $\gamma$  composition



for transpulmonary administration is housed in a vessel, and the fine particle powder are made using a device comprising means capable of applying the air impact to the freeze-dried composition in the vessel and means for discharging the resulting fine particle powder-form freeze-dried composition out of the vessel.

25. The transpulmonary administration method according to Claim 23, wherein the freeze-dried interferon- $\gamma$  composition for transpulmonary administration made into fine particles is administered to a user by inhalation by using the dry powder interferon- $\gamma$  inhalation system for transpulmonary administration according to any of Claims 15 to 18.

26. Use of a freeze-dried composition for transpulmonary administration by inhalation, wherein the freeze-dried interferon- $\gamma$  composition for transpulmonary administration according to any of Claims 1 to 14 is used by being formed into fine particles having a mean particle diameter of 10 microns or less or a fine particle fraction of 10% or more.

27. Use of the freeze-dried interferon- $\gamma$  composition for transpulmonary administration according to any of Claims 1 to 14 for manufacture of a dry powdered interferon- $\gamma$  preparation for transpulmonary administration by inhalation.